REMARKS/ARGUMENTS

The specification is amended herein to indicate that the present application claims priority to the U.S. provisional application serial no. 60/462,638, filed on April 11, 2003 by Blaney et al., entitled Compound Libraries and Methods for Drug Discovery. The pending claims are fully supported throughout the specification and claims in the April 11, 2003 provisional application as originally filed. For example, support for claim 50 is found on page 8, lines 27-29; page 40, lines 1-11; page 40, lines 16-17; page 41, lines 1-3; and page 41, lines 16-17; support for claim 57 is found on page 4, line 10 to page 5, line 2; support for claim 61 is found on page 12, lines 2-8; page 29, line 1 to page 31, line 21; support for claim 62 is found on page 29, line 11 to page 30, line 4; and support for claim 63 is found on page 4, line 10 to page 5, line 2.

Claims 50, 57 and 61-63 are pending in this application. The invention, as defined by these claims, is directed to a method of designing a lead candidate having biophysical or biochemical activity against a biological target molecule, comprising

a) Combining a crystalline biological target molecule with a mixture comprising at least two compounds, wherein at least one of said compounds comprises a substituent having anomalous dispersion properties;

b) Determining the structure of at least one of said compounds in association with said biological target molecule using x-ray crystallographic analysis; and

c) Selecting information from the structure to design said lead candidate.

Claim Rejections - 35 U.S.C. §103

The Action has rejected claims 50, 57 and 61-63 under 35 U.S.C. §103(a) as allegedly being *prima facie* obvious over the teachings of Dauter *et al., Acta Crystallographica D57:239-249 (2001),* in view of Congreve *et al., Agnew Chem. In. Ed. 42:4479-4482 (2003),* and/or Appleby *et al., Structure 7(6):629-641 (1999).* Applicants respectfully disagree.

Applicants first point out that Congreve is no longer prior art to the claimed invention. Congreve was published on September 25, 2003 whereas as amended herein, the pending application claims priority to U.S. provisional application serial no. 60/462,638, which

was filed on April 11, 2003. As described above, pending claims 50, 57 and 61-63 are fully supported by the specification and claims in the April 11, 2003 provisional application as originally filed.

The invention, as defined by the claims, distinguishes over Dauter by claiming a method of designing a lead candidate having biophysical or biochemical activity against a biological target molecule by combining a crystalline biological target molecule with a mixture comprising at least two compounds, wherein at least one of the compounds comprises a substituent having anomalous dispersion properties.

Dauter does teach or suggest any such methods. Instead, this reference teaches methods for phasing macromolecular structures for X-ray crystallography using halides. In particular, the structure of an enzyme known as pepstatin-insensitive carboxylase (PCP) from *Pseudomanas sp. 101* was solved by soaking crystals of PCP in sodium bromide, lithium sulfate and glycerol in Tris buffer solutions. As such, Dauter does not teach or suggest any methods for designing a lead candidate as claimed by the present invention. Absent a teaching or suggestion, one of ordinary skill in the art would not have been motivated to modify the teachings of the reference in order to arrive at the claimed invention. Nor would one of skill in the art have any reasonable expectation of successfully arriving at the claimed invention based on the teachings of this reference. Dauter teaches methods for phasing macromolecular structures whereas the claimed invention is directed to methods for designing a lead candidate. As such, this reference is directed to a different field of art than the claimed invention.

Appleby does not cure the defects of Dauter because this publication does not teach or suggest any methods for designing a lead candidate by combining a crystalline biological target molecule with a mixture comprising at least two compounds, wherein at least one of the compounds comprises a substituent having anomalous dispersion properties. Instead, this reference teaches solving the crystal structure of 5'-deoxy-5'-methylthioadenosine phosphorylase (MTAP) as well as the structure of MTAP with methylthioadenosine and sulfate ion soaked into the active site at 1.7 A resolution using multiwavelength anomalous diffraction phasing techniques. As such, Appleby does not teach or suggest any methods for designing a lead candidate as claimed by the present invention. Absent a teaching or suggestion, one of

ordinary skill in the art would not have been motivated to modify the teachings of Appleby or combine these teachings with Dauter in order to arrive at the claimed invention. Nor would one of skill in the art have any reasonable expectation of successfully arriving at the claimed invention based on the teachings of these references. Appleby teaches solving crystal structures of MTAP using multiwavelength anomalous diffraction phasing techniques, and Dauter teaches methods for phasing macromolecular structures. The claimed invention however, is directed to methods for designing a lead candidate. As such, Appleby and Dauter are directed to different fields of art than the claimed invention.

Applicants respectfully submit that a *prima facie* case of obviousness has not been established for the claimed invention and therefore, request reconsideration and removal of these rejections.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6155.

Respectfully submitted,

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